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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,915	01/21/2004	David Epstein	23239-547 (ARC-47)	6537

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EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	PAPER NUMBER
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/762,915	EPSTEIN ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *10,15,16,18-20,23-31 and 36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11-14,17,21,22,32-35 and 37-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 9/10/04, 3/14/06
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

An amendment was received on 11/29/06.

Claims 40 and 41 were added.

Applicant's election without traverse of group 1, the target TGFbeta2 and "SEQ ID NO: 107 (ARC238)" is acknowledged. It is believed that "ARC238" is a typographical error for ARC235, or possibly ARC283. See the specification at page 65, entry for SEQ ID NO: 107, and also Table 8 at page 67. The election is interpreted as an election of SEQ ID NO:107, since the term "ARC238" does not seem to appear in the specification as filed. Claims 10, 15, 16, 18-20, and 23-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/29/06.

In the response filed 11/29/06, Applicant indicated that claim 36 was withdrawn, even though it appears to be drawn to the elected invention. In the event that this was a typographical error, Applicant is advised that that all rejections set forth below that apply to claim 34, would also apply to claim 36 if rejoined.

Claims 1-41 are pending.

Claims 10, 15, 16, 18-20, 23-31, and 36 are withdrawn.

Claims 1-9, 11-14, 17, 21, 22, 32-35, and 37-41 are under consideration in this Action.

SEQ ID NO:107 is free of the prior art of record. The art rejections under 35 USC 102 and 103 set forth below are directed to the claims in their broad forms, not limited to SEQ ID NO:107.

Claims 13 and 14 read on embodiments in which the first and second aptamers are not the same. This is non-elected subject matter. Consistent with the restriction requirement of 5/30/06, Applicant's election does not allow for compositions comprising non-identical aptamers. Only embodiments of claims 13 and 14 which read on a single aptamer have been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 14-16 are indefinite because it is unclear what is intended by "type of target" or by "types of targets". This phrase could refer to different epitopes on the same molecule, or it could refer to different molecules, or to different classes of molecules (i.e. distinguishing enzymes from structural proteins, or proteins from lipids). The metes and bounds of the claims are unclear.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 11-15, 17, 32-35, 37, and 38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to the genus of aptamers that bind specifically to a any target involved in any way in any disorder of the eye.

The written description requirement may be satisfied for genus claims by disclosure of a representative number of species by reduction to practice or complete structural description, or by a disclosure of relevant identifying characteristics common to the species of the genus, such as a correlation between structure and function.

The instant specification discloses targets such as TGFbetas, PDGF, ICAM-1, IGF-1, VEGF, TNF-alpha, and integrin alpha 5 beta 3. Of these targets only TGFbeta and PDGF are correlated with specific diseases in the specification. The specification does not disclose any non-protein target molecule, and discloses only a handful of disorders (glaucoma, age related macular disorder, proliferative vitreoretinopathy, and proliferative diabetic retinopathy). Wistow et al (Mol. Vision 8:171-184, 2002) explored the expression profile of the human lens and found over 2000 non-redundant transcripts, novel gene, and splice variants. The specification as filed gives no guidance as to which of these transcripts is involved in any eye disease, and thus would

not convey to one of skill in the art that applicant was in possession of the genus of human lens protein targets involved in an eye disease, to say nothing of the genus of protein targets from all eye tissues involved in an eye disease, or of the even broader genus of all targets, (protein and non-protein) involved in eye disease. Accordingly, Applicant could not have been in possession of the genus of aptamers that bind specifically to a any target involved in any way in any disorder of the eye. Claims that specifically recite elected SEQ ID NO:107 (an aptamer specific for TGFbeta 2) are included in this rejection because the specification fails to adequately describe the genus of eye disorders in which TGFbeta 2 is involved.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-9, 11 13, 14, 21, 22, 32-35, 37, 40, and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Pagratis et al (WO 01/09156).

This rejection does not apply to the claims as limited by the elected sequence of SEQ ID NO:107, but applies to the claims as currently broadly written.

Pagratis taught pharmaceutical compositions comprising aptamer oligonucleotide ligands against TGFbeta-2. See abstract, page 5, lines 22-30, page 15, lines 13-16; and page 16, lines 8-13, and claims 1-8 on page 82. The compositions may comprise

non-aptamer biological agents such as nucleic acids, proteins, drugs, or other molecules, and may be conjugated to these molecules by a polyethylene glycol linker. See paragraph bridging pages 14 and 15. In addition one or more aptamers may be conjugated together in a complex. See paragraph bridging pages 12 and 13. Pagratis also taught a variety of other modifications to the aptamers, including substitutions at sugar, phosphate and base moieties. See paragraph bridging pages 17 and 18. The functional limitations recited in the claims are considered to be inherent in the structures of the aptamers or Pagratis. Since Pagratis taught aptamers that bind specifically to TGFbeta-2, the effects of binding are inherent absent evidence to the contrary.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 32, 37, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pagratis et al (WO 01/09156).

Pagratis taught pharmaceutical compositions comprising aptamer oligonucleotide ligands against TGFbeta-2. See abstract, page 5, lines 22-30, page 15, lines 13-16; and page 16, lines 8-13, and claims 1-8 on page 82. The compositions may comprise non-aptamer biological agents such as nucleic acids, proteins, drugs, or other molecules, and may be conjugated to these molecules by a polyethylene glycol (PEG)

linker. See paragraph bridging pages 14 and 15. In addition two aptamers may be conjugated together in a complex. See paragraph bridging pages 12 and 13.

Pagratis did not teach a composition comprising a linear arrangement of PEG-first aptamer-PEG-second aptamer. However, such an arrangement would have been obvious to one of ordinary skill in the art because Pagratis taught single PEGylated aptamers, as well as aptamers joined by a PEG linker, so the decision to link to pegylated aptamers together to obtain a linear arrangement of PEG-first aptamer-PEG-second aptamer is simply a matter of design choice.

Claims 1, 11, and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pagratis et al (WO 01/09156) in view of Cordeiro et al (Invest. Opthamol. Vis. Sci 40(10): 2225-2234, 1999).

Pagratis taught pharmaceutical compositions comprising aptamer oligonucleotide ligands against TGFbeta-2. See abstract, page 5, lines 22-30, page 15, lines 13-16; and page 16, lines 8-13, and claims 1-8 on page 82. The compositions may comprise non-aptamer biological agents such as nucleic acids, proteins, drugs, or other molecules, and may be conjugated to these molecules by a polyethylene glycol linker. The aptamers inhibit the function of TGFbeta-2. See page 36, lines 13-22.

Pagratis did not teach a composition comprising a TGFbeta-2 aptamer and an anesthetic agent, an anti-inflammatory agent, an anti-angiogenesis agent, an anti-proliferative agent, an anti-bacterial agent, an anti-viral agent, or an anti-fungal agent.

Cordeiro taught that mitomycin C was useful in the treatment of glaucoma, as were anti-TGFbeta-2 antibodies. Mitomycin-C is an antiproliferative antibiotic that inhibits DNA replication.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use both the aptamer of Pagratis and either or both of the antibody or mitomycin C of Pagratis together in the same composition to treat glaucoma. One would have been motivated to do so in order to obtain the benefits of both, or all three compounds, simultaneously. In view of the teachings of Cordeiro and Pagratis, one of ordinary skill in the art at the time of the invention would have had a reasonable expectation of success in using the aptamers of Pagratis to treat glaucoma. This is because Cordeiro taught that a monoclonal antibody against TGFbeta-2 was useful for this purpose, and because Pagratis found that an anti-TGFbeta-2 aptamer inhibits the TGFbeta-2 bioactivity with a potency equivalent to that of a monoclonal anti-TGFbeta-2 antibodies. See sentence bridging pages 39 and 40. Thus the invention as a whole was prima facie obvious.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the

hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, J. Douglas Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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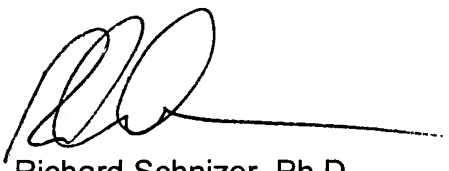

Richard Schnizer, Ph.D.
Primary Examiner
Art Unit 1635

S27391	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(20040253243.pn.) and target	2007-03-09 11:27:17
S27390	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	20040253243.pn.	2007-03-09 11:27:09
S27389	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(aptamer same (peg or polyethylene glycol)) and bivalent same aptamer	2007-03-09 10:20:14
S27388	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	(aptamer same (peg or polyethylene glycol)) and bivalent	2007-03-09 10:19:33
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S27384	U	PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD	6946292.pn.	2007-03-09 08:43:55
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			glaucoma or scar or scarring or intraocular or pressure)	07:52:39
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